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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FISH & RICHARDSON, PC
12390 EL CAMINO REAL
SAN DIEGO, CA 92130-2081

EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,739	CALLEN ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,11-16,29,47-92,95-107,111-115 and 117-124* is/are pending in the application.

4a) Of the above claim(s) *49-73,95-100,111-115 and 117-122* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,11-16,29,47,48,74-92,101-106,123 and 124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-03, 10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2, 5-6, 11-16, 29, 47-92, 95-107, 111-115, 117-124 are currently pending and are present for examination. Claims 1-2, 5-6, 11-16, 29, 47-48, 74-92, 101-106, 123-124 are now under consideration. Claims 49-73, 95-100, 111-115, 117-122 remain withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election with traverse of Group I, in paper filed on 10-7-04 is acknowledged. The traversal is on the ground(s) that coexamination of Group V and VI with Group I would not be burdensome to the Examiner. This is not found persuasive because as explained in the previous Office action, the search would require the search of classes and subclasses that are unnecessary for the search of group I. Furthermore, while the searches for the three groups overlap, they are not coextensive. For example, search of Group I would require search of subclass 435/200 while search of Group V and VI would require search of subclass 712/1.00. Next applicant also arguer that process claims in groups IV, VII-XI, XIII-XIX should also be rejoined. Examiner respectfully disagrees with the applicants that an argument is persuasive to overcome the restriction. These groups are distinct from the elected group until such time that the elected product is found allowable for reasons indicated in the previous Office action. Examiner has already indicated that inventions drawn to method of making and using the allowable product will be rejoined at that time. Therefore Examiner urges applicants to review their process claims and keep it free of enablement and description problems such that they can be easily rejoined by the Examiner when the product claims are found in condition of allowance.

The requirement is still deemed proper and is therefore made FINAL.

Claims 49-73, 95-100, 111-115, 117-122 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper filed on 10-7-04.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims c are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide with SEQ ID NO:1 encoding an enzyme of SEQ ID NO:2, having amylase activity, does not reasonably provide enablement for any polynucleotide comprising a polynucleotide having 70, 75, 80, 85, 90 or 95% sequence identity with SEQ ID NO:1 or a polynucleotide that is 70% identical to a sequence comprising 100 or 200 nucleotides of SEQ ID NO:1, or probes or oligonucleotides that comprise 10, 15, 20, 25, 30, 35, 40, 50, 75, 100 or 150 nucleotides of SEQ ID NO:1 or polynucleotides comprising sequences that are 90, 95, or 97% identical to 15 contiguous nucleotides of SEQ ID NO:1, or polynucleotides encoding

a polypeptide having 70% sequence identity with SEQ ID NO:2, vectors, host cells comprising the above and method of making the polypeptide encoded by said polynucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 5-6, 11-16, 29, 47-48, 74-92, 101-106, 123-124 are so broad as to encompass any polynucleotide comprising a polynucleotide having 70, 75, 80, 85, 90 or 95% sequence identity with SEQ ID NO:1 or a polynucleotide that is 70% identical to a sequence comprising 100 or 200 nucleotides of SEQ ID NO:1, or probes or oligonucleotides that comprise 10, 15, 20, 25, 30, 35, 40, 50, 75, 100 or 150 nucleotides of SEQ ID NO:1 or polynucleotides comprising sequences that are 90, 95, or 97% identical to 15 contiguous nucleotides of SEQ ID NO:1, or polynucleotides encoding a polypeptide having 70% sequence identity with SEQ ID NO:2, vectors, host cells comprising the above and method of making the polypeptide encoded by said polynucleotide. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino

acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single polynucleotide with SEQ D NO:1. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of SEQ ID NO: 1 as that encoding an amylase but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

On similar lines, claims directed to nucleic acid probes comprising oligonucleotides of at least 10 to at least 150 nucleotides can hybridize to any variant or mutant of SEQ ID NO:1 irrespective of whether the polynucleotide comprising the same encodes a polypeptide with SEQ ID NO:2. The specification does not teach as to how those skilled in the art can use the same to detect a polynucleotide with SEQ ID NO:1 or a polynucleotide encoding a polypeptide with SEQ ID NO:2.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide encoding an amylase with sequence identity as described above because the specification does not establish: (A) regions of the polynucleotide structure or the encoded polypeptide structure which may be modified without affecting their activity; (B) the general tolerance of amylase encoding polynucleotide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of the encoded polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides encoding an enormous number of amino acid modifications of the amylase with SEQ ID NO:2. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA

1970)). Without sufficient guidance, determination of amylase encoding polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 29, 74-91 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules.

The specification does not contain any disclosure of the function of all DNA sequences encoding a polypeptide having at least 70% sequence identity with SEQ ID NO:2 or the function of all those oligonucleotide probes claimed in claims 74-91. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 15, 16, 29, 47-48, 101-106, 123-124 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules comprising a polynucleotide having 70% sequence identity over a resgion of 100 nucleotides of SEQ ID NO:1 or encoding a polypeptide having 70% sequence identity over a regions of 100 amino acid residues of SEQ ID NO:2, vectors and host cells comprising the same and method of making said polypeptides.

These claims are directed to a genus of polynucleotides comprising a short structural similarity with SEQ ID NO:1 or 2. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the isolation and characterization of only a single species i.e., SEQ ID NO:1, 2. Moreover, the specification fails to describe any other representative species by sufficient identifying characteristics or properties to show that applicant was in possession of the claimed genus. The identifying characteristics

recited in above claims i.e., a polynucleotide having 70% sequence identity over a region of just 100 nucleotides of SEQ ID NO:1 or encoding a polypeptide having 70% sequence identity over a regions of 100 amino acid residues of SEQ ID NO:2, which together include structural description of about 5% of the structure of the single disclosed species (i.e. 70 nucleotides from the nearly 1400 nucleotides of SEQ ID NO:1), does not include sufficient characteristics to limit the claimed genus to polynucleotides which are not highly variable in both structure and function. The claims include species in which up to 95% of the polynucleotide sequence and up to 80% of the encoded amino acid sequence of the single disclosed species has been substituted as well as allowing alterations in functional characteristics such as substrate specificity, temperature optima, pH optima, and inhibitor/activator profiles. Therefore, the species within the genus are highly variable in both structure and function. As even small changes in structure can change any one of the properties of SEQ ID NO:1 or 2, inclusion of all of the members that fall in the instantly claimed genus together leads one to a conclusion that the recited genus is highly variable in structural or functional characteristics. Thus for all the reasons discussed, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 11, 15-16, 29, 47-48, 74-83, 86, 92, 101-106 are rejected under 35 U.S.C. 102(b) as being anticipated by Tachibana et al. (J. Ferment. Bioengg., 1996, Vol. 82(3):224-232, cited in the IDS and GenBank Accession No. O33476, Jan 1998). This rejection is based upon the public availability of printed publications. Claims 1, 2, 15-16, 29, 47-48, 74-83, 86, 92, 101-106 of the instant application are drawn to polynucleotides comprising a sequence having at least 70% sequence identity with SEQ ID NO:1 over a region of at least 100 nucleotides, or polynucleotide encoding a polypeptide having a 70% sequence identity with SEQ ID NO:2 over a region of 100 amino acid residue, polynucleotide which hybridizes to SEQ ID NO:1 under stringent conditions and encodes a polypeptide with amylase activity, polynucleotide comprising at least 10, 15, 20, 25, 3035, 40, 50, 75 contiguous nucleotides of a polynucleotide comprising a sequence having at least 70% sequence identity with SEQ ID NO:1 over a region of at least 100 nucleotides, vectors and host cells comprising the same and a method of making the polypeptide using said polynucleotide. Tachibana et al. disclose such a polynucleotide along with vectors, host cells and a method of making said polypeptide using said polynucleotide. See enclosed sequence alignment. Thus Tachibana et al. anticipate claims 1, 2, 11, 15-16, 29, 47-48, 74-83, 86, 92, 101-106 of this application as written.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the

examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

December 14, 2004